

Methamphetamine Abuse: An Overview for Health Care Professionals

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Methamphetamine is a stimulant and drug of abuse. Its use has shown a recent reemergence nationwide, most notably in Hawaii. Much of this increase is accounted for by smokable crystallized methamphetamine "ice". Its acute effects include cardiovascular and psychiatric disturbances. Chronically, structural and functional brain damage may occur. Psychosis may occur acutely or chronically, and sometimes even in abstinent patients.

Case Report

Ms. B. is a 30-year-old woman who presented to the emergency department of a major urban hospital in Hawaii, asking for "drug detox". She stated that she came in because she felt suicidal after relapsing from about 2 weeks of abstinence from crystal methamphetamine use. She had recently been admitted to an inpatient drug treatment facility, and had left against medical advice 3 days prior to presenting to the emergency department. She stated that she had felt that she was "strong enough to stay off ice"; however, she soon encountered someone with whom she had used ice in the past. Immediately thereafter, they went to buy and then smoke crystal methamphetamine (ice). The patient denied any other psychoactive drug use in the past 2 weeks. She presented at 6 am on a Sunday, about 6 to 8 hours after having last used ice.

Ms. B. admitted to problems with alcohol in the past, but denied using much alcohol since starting to smoke ice about 6 months ago. She had been seeing a psychiatrist for supportive psychotherapy.

She had recently separated from her husband and has been homeless since leaving the inpatient facility 3 days ago. Ms. B. reported that she had been staying with friends since then; she admitted that some of these friends also use ice. The patient stated that she was taking cimetidine for gastrointestinal reflux, but was on no other medications and had no other medical problems.

On physical exam, the patient was fatigued and somewhat disheveled. Her pulse was 126, blood pressure was 145 over 88, respirations were 24 per minute, and temperature was 100.4 degrees Fahrenheit. Her pupils were reactive and 5 mm bilaterally. She

exhibited no signs of head trauma. At rest, she had a fine tremor of the hands. She had mild hyperreflexia, but exhibited no focal neurological deficits, and the remainder of the exam was normal.

Behaviorally, the patient was noted to be restless and did not maintain eye contact. She was often uncooperative with the exam. Her speech was pressured, but normal in volume. Her mood was irritable; her affect was mood-congruent but constricted. She admitted to both auditory and visual hallucinations, stating that she had been seeing shadows and hearing voices which she described as "mumbo jumbo." Her thought processes were disorganized and often tangential. She was occasionally paranoid about various friends. She was oriented to person, but not to place or time. Cognitively, she exhibited markedly diminished memory for recent events. The patient did not exhibit violent tendencies, and she denied current homicidal ideation, but she did admit to throwing rocks at parked cars earlier in the morning. She also reported fleeting thoughts of jumping in front of a bus over the past 12 hours.

On laboratory examination, the patient's qualitative urine toxicology screen was positive for methamphetamine and benzodiazepines.

The patient was given risperidone, 1 mg orally, and was then observed in the emergency department for 3 hours. As she continued to exhibit suicidal and paranoid thoughts, she was admitted voluntarily to a locked psychiatric ward for treatment. She progressed well in the hospital and was discharged after 4 days with instructions to follow up with a rehabilitation program. The patient was subsequently lost to follow-up.

Introduction and History

Methamphetamine is a synthetic amine belonging to the amphetamine class of drugs. It has stimulating effects on both the central and peripheral nervous systems. Although they have been and continue to be prescribed by physicians, amphetamines are increasingly being used for illicit purposes, both in the U.S. and abroad. Unfortunately, although methamphetamine is a chemical that does not occur in nature, it is all too easy to obtain or to synthesize (detailed instructions for doing so can be obtained over the Internet).

Originally synthesized in 1887 by a German chemist, it was not until the 1930's that amphetamines became used therapeutically. During the 1930's and 40's, amphetamines of various types were promoted by American pharmaceutical companies as therapeutic for a number of ailments, supposedly without any risk of addiction. Over the same period, in Japan, large quantities of methamphetamine, mostly in pill form, were manufactured for domestic consumption. After the war, Japanese pharmaceutical companies followed the lead of their American counterparts, launching a large promotional campaign for over-the-counter methamphetamine pills that were in abundance at former military warehouses. Thus it came to be in Japan that the first large-scale epidemic of methamphetamine use occurred.¹

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In the U.S., where a prescription was still needed to legally obtain amphetamines, the epidemic was slower in coming. However, by the 1950's, nonmedical use of amphetamines had spread to the civilian population, mostly those in need of stimulation to keep awake or fend off boredom in repetitive or monotonous tasks. Not surprisingly, truck drivers, college students, athletes, and housewives made up the first major wave of amphetamine abusers in the U.S. At the same time, prescription amphetamines, including methamphetamine, continued to be promoted as therapeutic for hyperactivity, obesity, narcolepsy, and depression.²

In the 1960's, intravenous use of methamphetamine became more popular, especially among those who had already been using illicit drugs. This group was apparently the first to use methamphetamine solely for its euphoric effects, rather than for its stimulating or anorectic properties. This "second wave" of the American epidemic was largely held in check through law-enforcement and public health efforts to educate and treat abusers and potential users. Japan had similar campaigns, with particularly stiff penalties for drug manufacture or importation.³

However, by the mid-1980's in the U.S. (and even earlier in Japan), a rapid increase in methamphetamine abuse began. This "third wave" began with the introduction of a potent, smokable form of crystal methamphetamine, known as "crystal", "glass", or "ice" on the street. In the Philippines, and among the Filipino expatriate communities in the U.S. (especially in Hawaii), it has been known as *batu* (Tagalog for "rock").

This newer form has been gaining in popularity over the intravenous form due to its ease of use, and over the oral form due to its rapidity of CNS effect (and thus a more potent "high"). It has also attracted users of "crack" (smokable cocaine), due to the longer duration of the "high" or "rush". In fact, users of crack cocaine report being unable to distinguish the clinical effects of crystal methamphetamine (ice) from that of crack.⁴ In Hawaii, where crackdowns on marijuana production and sale have recently taken place, part of the boom in crystal methamphetamine use may be due to lesser availability of marijuana and other drugs.

Epidemiology

The routes of administration of methamphetamine include oral, intravenous, and by inhalation of its smoke. According to a study done in three American cities in 1994, the total number of users employing each of the three modes of use was nearly equal (i.e., one-third each). Of note, however, was that the percentage of methamphetamine users in the Honolulu group who preferred the smokable form was 92% (versus 10% for San Diego and 8% for San Francisco).⁵ This suggests an altogether different epidemic in Hawaii compared to the Mainland.

The reasons for this difference are unclear, but there are some other interesting differences between the usage patterns in Hawaii versus the Mainland: users in Honolulu were significantly younger, less educated, much more likely to come from a family in which the parents used marijuana or cocaine, and more likely to have begun using methamphetamine recently. Those in the Honolulu group were also more prone to violence, assaults, shoplifting, money problems, and weight loss.⁵

There were also differences in age and ethnic background, but it is difficult to assess whether this is due to the different composition of the Hawaiian population. In a study looking at ice users on Oahu, the using population was more likely to be young (59% under age 20, compared with only 30% in the population at large). Additionally, Filipinos, Hawaiians and part-Hawaiians were represented disproportionately (23% of users were Filipino versus 12.6% in the general population, while 35% were Hawaiian/Part-Hawaiian, who

represent just 10.7% of the population, according to census figures). Japanese, Korean, Chinese, Caucasian, Hispanic, and Black were all underrepresented ethnicities.⁶ However, it is worth keeping in mind that data for ethnic background were self-reported, and thus could be susceptible to bias.

Acute Effects

The acute clinical effects of all psychostimulants, including the amphetamines and cocaine, are strikingly similar.⁷ Methamphetamine differs in its sympathomimetic actions from other amphetamines in that it exerts fewer peripheral effects (e.g., tachycardia) and more CNS effects (e.g., euphoria), possibly due to a higher CNS penetration.²

The physical, or peripheral effects of methamphetamine are mediated by the autonomic nervous system and include: tachycardia, tachypnea, tremor, hypertension, dry mouth, mydriasis, and blurry vision. The mechanism for these effects appears to be methamphetamine's ability to stimulate release of norepinephrine at nerve terminals and of epinephrine from the adrenal medulla.⁸

Potentially lethal toxicities of methamphetamine overdose are most commonly seen in first-time users who take a single, large dose.⁸ Worrisome symptoms include hyperthermia, arrhythmias, and marked hypertension. Permanent neurological sequelae may also occur: cerebral infarcts can result from ischemia or hemorrhage secondary to a sudden, massive increase in blood pressure; also, direct neurotoxicity can result from central hyperthermia, which is easily exacerbated by increased muscular activity in agitated patients.² In addition, myocardial infarction and acute pulmonary edema have been associated with methamphetamine ingestion.^{9,10}

The central effects of methamphetamine apparently result from its structural similarity to the catecholamine neurotransmitters that are active in the CNS (e.g., epinephrine, norepinephrine, and dopamine).⁴ Behaviorally, users of methamphetamine report increased energy, perception, self-confidence, and sexuality, as well as a sense of euphoria.⁷ However, they also commonly experience irritability, impulsivity, impaired judgement, and insomnia, as well as such non-behavioral CNS effects as nausea, dizziness and anorexia. Psychotic behaviors such as hallucinations and paranoia are other potentially dangerous manifestations of acute toxicity, and can lead to irrational, suspicious, and often violent behavior, which may persist for days or even weeks.² The risk of homicidal or suicidal attempts is significant in such patients.¹¹ These patients pose a special challenge to care providers in the emergency setting, as the psychosis is often clinically indistinguishable from paranoid schizophrenia. One characteristic feature of these psychotic episodes is that, like drug-induced psychoses in general, they frequently involve vivid visual or tactile hallucinations.⁸

Chronic Effects

Chronic abuse of methamphetamine can lead to neuron loss secondary to microvascular damage, as well as to a depletion of dopaminergic neurons, both of which may be permanent.⁸ An example of a sequela that may be due to this effect on dopaminergic neurons, ostensibly on those in the substantia nigra, is the movement disorders that are sometimes seen in patients using methamphetamine, as well as in those who have quit.

Another effect of chronic abuse of methamphetamine is the CNS "kindling" phenomenon, also referred to as "reverse tolerance". Patients who have used amphetamines over a long period, especially those who have had psychotic episodes from its use, may be pushed into a frank psychosis by even very small amounts of an amphetamine (or indeed by any psychostimulant, including caffeine and nicotine).^{8,12} The mechanism for this kindling phenom-

enon is uncertain, but it may involve alterations in dopaminergic sensitivity of the striatum.⁸ This is discussed further in the next section.

Some investigators also point to the existence of a chronic psychosis, termed "withdrawal" or "abstinence" psychosis, secondary to long-term use of amphetamines. However, some believe that these patients should be considered to have had latent schizophrenia that may have been brought out, rather than caused *de novo*, by amphetamine use.^{13,14}

Tolerance and Sensitization

Tolerance develops for some of the effects of methamphetamine, especially those acting via the peripheral nervous system, as well as for certain CNS effects (such as euphoria, anorexia, and hyperthermia).⁷ However, the reverse is true for effects on judgement, impulsivity, aggression, and susceptibility to paranoia, delusions, and hallucinations. In other words, while it takes more and more drug to achieve a desired high, and while these users acquire a decreased sensitivity to tachycardia and hypertension, they are actually more likely to exhibit pathological, often violent or self-destructive behavior even with no escalation in dose (or indeed with a decrease).⁸ This sensitization illustrates the effect of the kindling concept mentioned above. Further, since tolerance develops relatively rapidly, users often end up at doses 50 or 100 times greater than the dose they began with. Although they are physically better able to handle these massive doses than would be a drug-naïve subject, psychologically they are actually less so. In fact, the relative lack of significant physical effects may give some users a false sense that they can "handle" the dose.

Addiction and Withdrawal

The degree to which methamphetamine is addictive depends greatly on the type and route of administration. Methamphetamine taken by a method that delivers a large bolus of active drug to the brain all at once, such as the IV or smokable forms, gives a much more intense, albeit shorter-acting, euphoria than does the 'traditional' oral form. Both of these pharmacodynamic differences contribute to the stronger potential for addiction of the rapid-acting formulations: users of these forms get the most positive reinforcement for taking the drug, due to stronger associations between administering the drug and experiencing pleasurable feelings. Thus, smoked methamphetamine (ice) is, as one would expect, much more addictive than oral methamphetamine, which is in turn twice as addictive as amphetamine.²

One would also expect smokable methamphetamine to be similar in its addictive potential to smokable cocaine (crack), given that their euphoric effects are virtually indistinguishable. However, the duration of euphoria with ice smoking is much longer than it is for crack smoking (subjective half-life is about 5 hours for methamphetamine, versus only about 50 minutes for cocaine).⁸ This difference would be expected to cause crystal methamphetamine to be less addictive than crack, but this remains to be proven in humans.

Patients who are dependent on methamphetamine and then discontinue use suddenly are prone to both psychological and physical withdrawal. The psychological reaction can vary from vague feelings of malaise to cravings to extreme agitation or depression. Later, more physical symptoms, such as polyphagia and hypersomnolence commonly occur. Depressed mood and energy level may be protracted for as long as 4-6 months in severely dependent patients.² Patients frequently return to using amphetamines partly as a way of dealing with these withdrawal symptoms, even after their craving for the drug is gone.

Treatment

The road to recovery in methamphetamine abuse, as with any psychoactive substance, is a long and treacherous one. Initial efforts focus on gathering information and treating acute symptoms, especially psychosis and cravings, as well as acute medical conditions brought on by methamphetamine use. As the patient progresses through the various stages of recovery, increasing emphasis is placed on social and behavioral interventions.

The first 4 to 6 days after the patient's most recent methamphetamine use represent the detoxification period. This may be undergone as an inpatient if the patient is significantly toxic. Early in this interval, it is essential that a full medical workup be performed, as many of the acute effects of amphetamines are potentially lethal. Vital signs should be checked frequently, and blood pressure controlled to prevent end-organ damage. Initially, an EKG should be obtained on all patients with signs of toxicity; such patients may also need to be placed on seizure precautions.

If the patient is acutely suicidal, homicidal, or floridly psychotic, he or she may require admission to a locked psychiatric ward. In patients with significant agitation or current psychotic features, risperidone, 1 mg orally, or haloperidol, 1-2 mg intramuscularly, may be given every 12 hours as needed. If drug craving is the major problem, as evidenced by hypothermia and subjective reports from the patient, low-dose amantadine or bromocriptine may be tried, although these can bring out or aggravate psychotic features. Conversely, neuroleptics can induce increased drug craving. A less effective, but often better-tolerated treatment for craving is to replenish amino acids needed in the synthesis of neurotransmitters depleted by chronic stimulant use; these are marketed as combination preparations such as Tropamine and Renew.¹⁵ Acute abstinence-induced depression can sometimes be aborted by any of the tricyclic or serotonin-specific antidepressants, the latter being preferred for their relative lack of cardiac effects.

After the first week or so, the patient has largely recovered from the physiologic part of the addiction, and nonmedical interventions become foremost in importance to combat the psychological addiction, which is often much more problematic. These interventions may include daily twelve-step meetings, changing one's life-style to eliminate contact with friends who use, and making specific goals and commitments to maintain abstinence. By this stage, success is largely in the hands of the patient, and many patients relapse and start the process over many times before achieving a sustained recovery.

Conclusions

The Hawaiian epidemic of smokable crystal methamphetamine represents a serious public health and public safety threat. It remains to be seen whether this represents cultural and socioeconomic conditions unique to Hawaii, or whether this is merely the first outbreak of a national pandemic. Some signs point to the latter, including recent increases in use of smokable methamphetamine in West Coast cities.¹⁶ It will be extremely important to monitor usage patterns in Hawaii and on the Mainland in order to help formulate effective public health and law enforcement policies.

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the top. I turned to discover he was covering both eyes.

Richard Klein, *Toronto Stitches*
September '96

Quotable Quotes

"I feel that if I stop working I'll get old. My father, **Dr Sidney Kirby**, used to say that when he was still working in his 80's. (Mid Pac CC "Rub of the Green" member profile Claire Simpson quote). (Sidney Kirby was medical director at Kalaupapa in the 1950's and died in 1981 when he was 96-years-old).

"When a man sits with a pretty girl for an hour, it seems like a minute. But let him sit on a hot stove for a minute—and it's longer than any hour. That's relativity." *Albert Einstein*

(Gleaned from the *Medical Arts Press Newsletter Sept/Oct 96*)

"If you want to recapture your youth, just cut off his allowance." *Al Bernstein*

"Music washes away from the soul the dust of everyday living." *Leopold Stokowski*

"The best executive is the one who has sense enough to pick good men to do what he wants done, and self restraint enough to keep from meddling with them while they do it."

Theodore Roosevelt

"Which pharmaceuticals company will find a sure cure for impotence?" asks comic Paul Ryan.

"Speaking for joke writers everywhere, I hope it's Upjohn."

Quoted in Los Angeles Times

A candidate came home late one night and gave his wife the glorious news.

"Darling, I've been elected!"

"Honestly?" she replied exuberantly.

"Hey," he said, "why bring that up?"

Contributed by Cathryn Hopkins

Overheard: "The trouble with getting to work on time is that it makes the day so long."

Edgar Argo in National Enquirer

"Youth is a wonderful thing. What a crime to waste it on children."

George Bernard Shaw

Points to Ponder

Young writers often suppose that style is a garnish for the meat of prose, a sauce by which a dull dish is made palatable. Style has no such separate entity; it is nondetachable, unfilterable. The beginner should approach style warily, realizing that it is himself he is approaching, no other; and he should begin by turning resolutely away from all devices that are popularly believed to indicate style—all mannerisms, tricks, adornments. **The approach to style is by way of plainness, simplicity, orderliness, and sincerity.**

E.B. White "Elements of Style"

Sketches from Stitches

What Can You Say?

Recently one of my well known middle aged female patients presented urgently to the office.

"I have a headache," she said, "but I don't know what it is because there isn't much in there to hurt."

Marie Cescon MD, Woodville Ont.

High Tech Exam

John, yet in his 30's was concerned about prostate cancer. His father was found to have the condition and he had spent hours in a urologist's office reading pamphlets on prostate cancer and its prevention.

"I'm sorry," he said, "but could you tell me what tests I need to check for prostate cancer."

"A blood test and a rectal exam," I repeated.

"OK, OK, But if I'm really at risk, I don't want just any rectal exam. I want one of those new digital ones"

I.W. Tobson MD, White Rock, B.C.


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